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TRANSMITTAL
FORM

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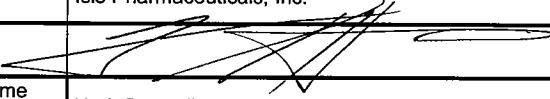
Total Number of Pages in This Submission

Patent Number	7,125,975
Issue Date	10/24/2006
First Named Inventor	Muthiah Manoharan
Title	DERIVATIZED OLIGONUCLEOTIDES HAVING IMPROVED UPTAKE AND OTHER PROPERTIES
Total Number of Pages in This Submission	6
Attorney Docket Number	ISIS-5425

ENCLOSURES (Check all that apply)

<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance Communication to TC
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Amendment/Reply	<input type="checkbox"/> Petition	<input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> After Final	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Power of Attorney, Revocation	<input type="checkbox"/> Status Letter
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<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Terminal Disclaimer	<input type="checkbox"/> Certificate of Correction
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<input type="checkbox"/> Reply to Missing Parts/ Incomplete Application	<input type="checkbox"/> Landscape Table on CD	
<input type="checkbox"/> <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53		
Remarks		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Isis Pharmaceuticals, Inc.		
Signature			
Printed name	Herb Boswell		
Date	11/13/2006	Reg. No.	27,311

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

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This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7,125,975

Page 1 of 5

APPLICATION NO.: 10/755,166

ISSUE DATE : 10/24/2006

INVENTOR(S) : Muthiah Manoharan, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

1) Title Page:

Item [60], Related U.S. Application Data, please delete

"Continuation of application No. 10/073,718, filed on Feb. 11, 2002, now Pat. No. 6,831,166, which is a division of application No. 09/633,659, filed on Aug. 7, 2000, now Pat. No. 6,395,492, which is a division of application No. 08/211,882, filed on Apr. 22, 1994, now Pat. No. 6,153,737, which is a continuation-in-part of application No. PCT/US92/09196, filed on Oct. 23, 1992."

and insert therefore

--Continuation of application No. 10/073,718, filed on Feb. 11, 2002, now Pat. No. 6,831,166, which is a division of application No. 09/633,659, filed on Aug. 7, 2000, now Pat. No. 6,395,492, which is a division of application No. 08/211,882, filed as application No. PCT/US92/09196 on Oct. 23, 1992, now Pat. No. 6,153,737.;

2) Column 6, line 21, please delete "B6" and insert therefore --B₆--;

3) Column 9, line 61, please delete ":";

4) Column 10, line 12, please delete "-";

5) Column 10, line 54, please delete "Bas" and insert therefore --Base--;

6) Column 11, line 58, please delete "." after "treated";

7) Column 12, line 13, please delete "C_sT_sG_s T_sC_sT_s C_sC_sA_s T_sC_sC_s T_sC_sT_s T_sC_sA C_sT" and insert therefore --C_sT_sG_s T_sC_sT_s C_sC_sA_s T_sC_sC_s T_sC_sT_s T_sC_sA_s C_sT--;

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 1896 Rutherford Rd.
 Carlsbad, CA 92008

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ISSUE DATE : 10/24/2006

INVENTOR(S) : Muthiah Manoharan, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

- 8) Column 15, line 47, please delete "is"" and insert therefore --"s"--;
- 9) Column 17, line 14, please delete "Na₂CO_{3/1}M" and insert therefore --Na₂CO_{3/1}M--;
- 10) Column 17, line 44, please delete "Na₂HCO_{3/1}M" and insert therefore --Na₂HCO_{3/1}M--;
- 11) Column 19, please delete

“
TABLE 1

HPLC Retention Times Of Oligonucleotides Functionalized
At 2' Position

Oligomer	Retention Time Minutes	
	Mono Substitution	Multiple Substitution
Oligomer 12 ¹	21.78	
Oligomer 13 ¹	22.50	
Oligomer 19 ²	23.58	
Oligomer 20 ²	24.16 ^a	25.19 ^b
Oligomer 21 ³	26.65	
Oligomer 22 ³	26.99 ^a	29.33 ^b
	27.55 ^a	
Oligomer 23 ⁴	30.10	
Oligomer 24 ⁴	30.38 ^a	37.00 ^b
	32.22 ^a	
Oligomer 25 ⁵	28.06	
Oligomer 26 ⁵	28.14 ^a	33.32 ^b
	29.24 ^a	

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ISSUE DATE : 10/24/2006

INVENTOR(S) : Muthiah Manoharan, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

and insert therefore

TABLE 1

**HPLC Retention Times Of Oligonucleotides Functionalized
At 2' Position**

Oligomer	Retention Time Minutes	
	Mono Substitution	Multiple Substitution
Oligomer 12 ¹	21.78	
Oligomer 13 ¹		22.50
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Oligomer 20 ²		24.16 ^a 25.19 ^b
Oligomer 21 ³	26.65	
Oligomer 22 ³		26.99 ^a 29.33 ^b 27.55 ^a
Oligomer 23 ⁴	30.10	
Oligomer 24 ⁴		30.38 ^a 37.00 ^b 32.22 ^a
Oligomer 25 ⁵	28.06	
Oligomer 26 ⁵		28.14 ^a 33.32 ^b 29.24 ^a
		--;

12) Column 21, line 14, please delete "Prot in-Conjugated" and insert therefore --Protein-Conjugated--;

13) Column 21, line 27, please delete "'is'" and insert therefore --"s"--;

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Page 4 of 5

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ISSUE DATE : 10/24/2006

INVENTOR(S) : Muthiah Manoharan, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

14) Column 22, please delete

“
TABLE 2
OLIGONUCLEOTIDE ANALYSIS VIA ENZYMATIC DIGESTION

Oligomer	Abs. max.	<u>Observed Ratios</u> **				
		267	252	267	260	
		C	G	T	A	A
Oligomer 10		2	1		1	
Oligomer 11		3	5	2	1	
Oligomer 12		9	1	8	1	1
Oligomer 13		9	1	8	2	“

And insert therefore

--
TABLE 2
OLIGONUCLEOTIDE ANALYSIS VIA ENZYMATIC DIGESTION

Oligomer	Abs. max.	<u>Observed Ratios</u> **				
		267	252	267	260	
		C	G	T	A	A
Oligomer 10		2	1		1	
Oligomer 11		3	5	2	1	
Oligomer 12		9	1	8	1	1
Oligomer 13		9	1	8	2	--;

15) Column 24, line 46, please delete “phase-HPLC” and insert therefore --phase HPLC--;

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**UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION**Page 5 of 5

PATENT NO. : 7,125,975

APPLICATION NO.: 10/755,166

ISSUE DATE : 10/24/2006

INVENTOR(S) : Muthiah Manoharan, et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

- 16) Column 29, line 7, please delete "solution-of" and insert therefore --solution of--;
- 17) Column 39, line 19, please delete "3" and insert therefore --30--;
- 18) Column 46, Claim 5, lines 32-33, please delete "5'-position" and insert therefore --5'-O-position--.

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